

(19) JAPANESE PATENT OFFICE (JP)

(12) **Official Gazette for Unexamined Patent Applications (A)**

(11) Japanese Unexamined Patent Application
(Kokai) No. Hei 9-25213

(43) Disclosure Date: 28 January 1997

(51) Int.Cl. ⁶	Ident. Symbols	Internal Office Nos.	FI	Technology Indication
A61K	7/00		A61K	7/00 K U X
	7/48			7/48
	35/78	ADA		35/78 ADA

Request for Examination: Not yet requested Number of Claims: 5 FD (Total of 10 pages) Continued on last page

(21) Application No.: Hei 7-200470	(71) Applicant: 000001959 Shiseido Company, Ltd. 5-5 Ginza 7-chome, Chuo-ku, Tokyo-to
(22) Application Date: 13 July 1995	(72) Inventor: Yuzo Yoshida c/o First Research Center, Shiseido Company, Ltd. 1050 Nitsuba-cho, Kohoku-ku, Yokohama-shi, Kanagawa-ken
	(72) Inventor: Naomi Tanaka c/o First Research Center, Shiseido Company, Ltd. 1050 Nitsuba-cho, Kohoku-ku, Yokohama-shi, Kanagawa-ken
	(72) Inventor: Eiichiro Yagi c/o First Research Center, Shiseido Company, Ltd. 1050 Nitsuba-cho, Kohoku-ku, Yokohama-shi, Kanagawa-ken
	(74) Agent: Chieko Tateno, Patent Attorney Continued on last page

(54) [Title of the Invention] **Skin Preparation for Topical Use**

(57) [Abstract]

[Objective] To provide a skin preparation for topical use having superior effects on color lightening and whitening in pigment deposition after sunburn, spots, freckles and liver spots, which is superior in protease inhibiting action and which is also effective in improving various skin diseases, skin roughness and chapping.

[Structure] A skin preparation for topical use in which extracts of plants of the genus *Scapium* of the family *Sterculiaceae* such as Buah tempayang (scientific name, *Scapium affinis* Pierre) are compounded.

[Claims]

[Claim 1] A skin preparation for topical use characterized in that extracts of plants of the genus *Scapium* of the family *Sterculiaceae* are compounded.

[Claim 2] A skin preparation for topical use as described in Claim 1 in which the plant of the genus *Scapium* of the family *Sterculiaceae* is Buah tempayang (scientific name, *Scapium affinis* Pierre).

[Claim 3] A skin preparation for topical use as described in Claim 1 or 2 which is a whitening agent for topical use.

[Claim 4] A skin preparation for topical use as described in Claim 1 or 2 which is a topical agent for improving skin roughness.

[Claim 5] A skin preparation for topical use as described in any of Claims 1 to 4 in which the compounding quantity of the extract of the plant of the genus *Scapium* of the family *Sterculiaceae* is 0.005 to 20.0 weight %.

[Detailed Description of the Invention]**[0001]**

[Field of Industrial Use] This invention relates to a skin preparation for topical use in which extracts of plants of the genus *Scapium* of the family *Sterculiaceae* are compounded. In greater detail, it relates to skin agents for topical use that inhibits production of melanin, that is effective in the prevention and improvement of pigment deposition after sunburn, spots, freckles and liver spots and that has improving and preventive effects on various skin diseases such as contact dermatitis and psoriasis, and, in addition, in skin roughness and chapping due to drying and detergents.

[0002]**[Prior Art and Problems the Invention is Intended to Solve]**

There are some points in regard to the mechanism of occurrence of skin spots and other conditions that are not clear. However, in general, it is thought that melanin pigment is formed because of hormonal abnormalities and irritation by ultraviolet rays from sunlight and that it is abnormally deposited in the skin. Melanin pigment, which is the cause of coloration of the skin, is produced in melanin-producing granules in the melanin cells (melanocytes), which are present between the epidermis and the dermis, and the melanin that is produced is diffused to adjacent cells by osmotic action. The biochemical reactions in the melanocytes are presumed to be as follows. Specifically, the process of production of melanin pigment is a process in which tyrosine, which is an essential amino acid, is transformed to dopaquinone by the action of the enzyme tyrosinase and in which the dopaquinone is changed to black-colored melanin via a red pigment and a colorless pigment by enzymatic and non-enzymatic oxidation. Consequently, inhibition of the action of tyrosinase, which is the first stage of the reaction, is important in production of melanin.

[0003] However, the effects of compounds that inhibit the action of tyrosinase, except for hydroquinone, are manifested extremely slowly, for which reason its improving effect on pigment deposition in the skin is not sufficient. On the other

hand, although the effect of hydroquinone is seen evenly, because sensitization to it occurs, its use is generally restricted. Therefore, in order to increase its safety, attempts have been made to convert it to monoesters and alkyl monoethers of higher fatty acids (Japanese Patent Application Sho 58-143507 [1983]). However, because esters are decomposed in the body hydrolases, it is difficult to say that they are of sufficient safety. In addition, ethers that are satisfactory from the standpoint of safety cannot be obtained.

[0004] In recent years, it has been ascertained that proteases contribute to the development of morbid states in various skin diseases. For example, in psoriasis, which is representative of inflammatory abnormal keratinization diseases, high plasminogen activator (PA) activity is found in the afflicted epidermis. PA is a serine protease and Haustein has reported that intense PA activity is present in psoriatic epidermis, particularly in sites of disordered keratinization (Arch.Klin.Exp.Dermatol; 234, 1969). Fraki and Hopsu-Havu extracted PA activity from the scaly layer of psoriasis using high concentration salt solution (Arch.Dermatol.Res; 256, 1976). In addition, it has been ascertain in *in vitro* experimental systems that, in chronic pemphigus, PA, which is synthesized in large quantities in the epidermal cells, converts plasminogen that is present outside the cells to plasmin, which digests intercellular binding substances with the result that tissue fluids are retained in the cells and that vesicles are formed in the epidermis (Morioka S. et al: J.Invest.Dermatol; 76, 1981). It is further believed that proteases play an important role in normal keratinization processes such as formation of the keratin layer (Ogawa H., Yoshiike T: Int.J.Dermatol; 23, 1984) and attempts have been made to use protease inhibitors for skin improvement and as therapeutic drugs for skin diseases.

[0005]

[Problems the Invention is Intended to Solve] In the light of the circumstances described above, the inventors studied the inhibitory effects on melanin production and the protease inhibitory activity of a wide variety of substances. As the result, it was discovered that extracts of plants of the genus *Scapium* of the family *Sterculiaceae* have an inhibitory action on melanin production and a protease inhibitory action. In addition, it was discovered that said plant extracts are extremely effective in improving skin roughness. There have been no reports up to this point on the melanin production inhibitory activity of plants of the genus *Scapium* of the family *Sterculiaceae* and their application as beautifying agents and agents for improvement of skin roughness is completely unknown. Moreover, there are no examples of compounding plants of the genus *Scapium* of the family *Sterculiaceae* in topical skin preparations. The inventors perfected this invention on the basis of the above-described findings.

[0006] Specifically, this invention is a skin preparation of topical use characterized in that plants of the genus *Scapium* of the family *Sterculiaceae* are compounded.

[0007] We shall now describe the structure of this invention. The plant of the genus *Scapium* of the family *Sterculiaceae* is, ideally, for example, Buah tempayang; (scientific name: *Scapium affinis* Pierre). It is a plant that is produced in dry grasslands and pastures in Indonesia in particular. The extracts that are used in this invention are obtained by soaking or heating and refluxing all parts of the above-described plant such as its leaves, bark, stalks, including underground stalks, and fruits together with an extraction solvent, after which the parts are filtered and concentrated. The extraction solvents that are used in this invention can be any solvent as long as it is a solvent that is ordinarily used in extraction. In particular, alcohols such as methanol and ethanol, alcohols containing water and organic solvents such as acetone and ethyl acetate can be used individually or in combinations.

[0008] The quantity of extract of plants of the genus *Scapium* of the family *Sterculiaceae* that is compounded should be 0.005 to 20.0 weight %, and, preferably, 0.01 to 10.0 weight %, as dry substance in the total quantity of the topical preparation. When it is less than 0.005 weight %, the effect of this invention is not sufficiently manifested. When it exceeds 20.0 weight %, preparation is difficult, which is not desirable. In addition, a greater effect is not improved as the amount compounded increases over 10.0 weight %.

[0009] The skin preparation for topical use of this invention is ideal for applications as whitening agents, skin roughness improving agents and protease inhibitors. The term protease of protease inhibitors is a general term for enzymes that catalyze hydrolysis of peptide bonds, which proteases are classified as peptidases and proteases. The former are enzymes that sever peptide bonds from the outer sides of the amino group terminals and the carboxyl group terminals of peptide chains and the latter are enzymes that cut specified bonds in the peptide chain. The latter proteases are generally classified into four types, serine systems, cysteine systems, aspartic acid systems and metal systems, depending on the type of active catalytic group. Specific inhibitory agents exist for each of them. The protease inhibitors in this invention are characterized in that they exhibit inhibitory activity specifically against serine protease.

[0010] In addition to the above-described essential constituents, constituents which are ordinarily used in skin preparations for topical use such as cosmetics and medicinal drug products, for example, other whitening agents, humectants, antioxidants, oleaginous constituents, ultraviolet ray absorbents, surfactants, thickeners, alcohols, powder components, colorants, aqueous constituents, water and various skin nutrients may appropriately be compounded as required in the skin preparation for topical use of this invention.

[0011] In addition, metallic blocking agents such as sodium edetate, trisodium edetate, sodium citrate, sodium polyphosphate, sodium metaphosphate and gluconic acid, drug preparations such as caffeine, tannin, verapamil, tranexamic acid and derivatives thereof, licorice extract, glabridine, hot water extract of [?] seeds, various types of

natural drugs, tocopherol acetate, and glycyrrhizic acid and derivatives or salts thereof, other whitening agents such as vitamin C, magnesium phosphate ascorbate, ascorbic acid glucosides, arbutin and kojic acid and saccharides such as glucose, fructose, mannose, sucrose and trehalose can be compounded appropriately.

[0012] The skin preparation for topical use of this invention may be any preparation form as long as it is conventionally used in skin preparations for topical use such as, for example, an ointment, a cream, an emulsion, a lotion, a pack, or a bathing preparation.

[0013]

[Working Examples] We shall now describe this invention in greater detail by means of working examples. This invention is not limited by them. The compounding quantities are weight %. Prior to the working examples, we shall describe (1) the melanin inhibiting effect, the tyrosinase activity inhibiting effect and the whitening effect and (2) the test methods and results thereof for the protease inhibiting effect and the skin roughness improving effect of the plant extracts of this invention.

[0014] (1) Test methods and results thereof for melanin inhibiting effect, the tyrosinase activity inhibiting effect and the whitening effect

1. Preparation of Test Materials

50 g of fruit parts of Buah tempayang was immersed for one week at room temperature in ethanol, the extraction solution was concentrated and 2.7 g of ethanol extract was obtained. This extract was dissolved in 1% of DMSO, this solution was diluted to adjust its concentration and the following experiments were conducted using it.

[0015] 2. Cell Culture Method

B16 melanoma culture cells originating from mice were used. They were cultured at 37°C in a CO₂ incubator (95% air, 5% carbon dioxide) in Eagle's MEM culture medium containing 10% FBS and theophylline (0.09 mg/ml). After culturing for 24 hours, the test material solution was added to give a final concentration (concentration converted for dry extract) of 10⁻² to 10⁻⁵ weight %, culturing was continued for 3 days and visual evaluation of the quantity of melanin production and determination of tyrosinase activity inhibitory effect were performed by the following methods.

[0016] 3. Visual Determination of Melanin Quantity

Diffusion plates were placed on the covers of the well plates, the quantity of melanin in the cells was observed with an inverted microscope and a comparison was made of the case of a test material (reference) to which plant extract was not added. The result are shown in Table 1. As a reference, the same test as described above was performed for an extract of keigai [*Schizonepeta tenuifolia*](Subclass *Lamioideae* of the family *Labiatae*) of which the melanin production inhibiting action was known. The results are shown in Table 1. **[Translator's Note:** "Keigai" is the Japanese reading for a traditional Chinese medicinal plant and is to be found on the

Internet with the reading “keigai.” This version will be used in the subsequent translation.]

[0017] < Evaluation Standards >

O: White (quantity of melanin)

Δ: Somewhat white (quantity of melanin)

×: Reference (melanin quantity)

[0018] 4. Determination of Tyrosinase Activity

The culture medium in the cells before determination was removed and it was washed two times with 100 μl of PBS. PBS containing 45 μl Triton-X (surfactant, brand name manufactured by the Rohm and Haas Company) was added to each well. The plate was agitated for 1 minute to thoroughly destroy the cell membrane. On microplate return, absorbance at 475 nm was determined and was taken as absorbance at 0 minutes. Following that, 5 μl of 10 mM L-

Dopa solution was rapidly added, the solution was transferred to an incubator at 37°C and a reaction was carried out for 60 minutes. The plate was agitated for 1 minute and absorbance (475 nm) at 60 minutes was determined. The percentage of the difference in the above-described absorbance in the test material to which plant extract was added relative to the difference in absorbance at 0 minutes and 60 minutes for the test material to which plant extract was not added (control) was taken as the tyrosinase activity ratio (%). The results are shown in Table 1. As a reference example, the same test as described above was performed for an ethanol extract of *keigai* of which the tyrosinase activity inhibitory action was already known. In the table, - signifies that a significant difference was found at a level of significance of less than 5% by comparison to the control.

[0019]

[Table 1]

Test	Visual Evaluation of Melanin Production				Tyrosinase Activity Ratio (%)			
	10 ⁻⁵	10 ⁻⁴	10 ⁻³	10 ⁻²	10 ⁻⁵	10 ⁻⁴	10 ⁻³	10 ⁻²
Concentration (weight %)								
Buah tempayang extract	×	×	×	O	72	72	75	47
Keigai extract	×	×	×	×	-	-	-	55

[0020] 5. Whitening Effect Test

[Test Method] Skin on the inner side of the upper arm of 40 test subjects that had been exposed for 4 hours (2 hours a day for 2 days) to sunlight during summer was used as the subject of the tests. Each test material was applied once each (Alcohol phase)

95% ethyl alcohol	55.0 weight %
Polyoxyethylene (25 mol) hardened castor oil ether	2.0
Preservative – antioxidant	suitable quantity
Fragrance	suitable quantity
Drug preparation (recorded in Table 2)	
(Aqueous phase)	
Glycerol	5.0
Sodium hexametaphosphate	suitable quantity
Ion exchange water	remainder

in the morning and evening for 4 weeks beginning 5 days after the day of exposure to sunlight. The panel was divided into 8 persons per group to make 5 groups and tests were performed with the formulations indicated below.

< Preparation method > The aqueous phase and the alcohol phase were prepared separately, after which the two phases were mixed and solubilized.

[0021] [Evaluation method] The color lightening effect after use was evaluated on the basis of the evaluation standards indicated below.

Ø: Cases in which the proportion of subjects in which it was markedly effective and effects was 80% or higher

O: Cases in which the proportion of subjects in which it was markedly effective and effects was 50% to 80%

Δ: Cases in which the proportion of subjects in which it was markedly effective and effects was 30% to 50%

×: Cases in which the proportion of subjects in which it was markedly effective was 30% or less

[0022] Test materials comprised of compounding compositions described in the above-described test method were prepared and the whitening effects were compared using the drug preparations described in Table 2.

[0023]

[Table 2]

Drug Preparation	Compounding Quantity (Weight %)	Effect
No addition	-	×
Hydroquinone	1.0	Δ
Buah tempayang extract	0.1	O
Buah tempayang extract	1.0	O
Buah tempayang extract	10.0	Ø

[0024] The Buah tempayang extract indicated in Table 2 was obtained by adding fruit of Buah tempayang to ethanol and subjecting it to heating and reduction, after which it was filtered, concentrated and dried.

[0025] As should be evident from Table 2, it was found that the effect after exposure to the sun was that addition of Buah tempayang extract prevented deposition of excess melanin pigment and prevented blackening.

[0026] (2) Test methods and results for tyrosinase inhibiting effect and roughness improving effect

1. Test of Proteinase Inhibiting Effect

Inhibitory activity of two representative serine proteases, plasmin and trypsin, was evaluated.

[0027] (1) Preparation of Test Materials

The fruit part of Buah tempayang was immersed in ethanol at room temperature for 1 week and the extraction solution was concentrated and dried. The dried product was dissolved in ethanol and a 1% ethanol solution was prepared.

[0028] (2) Determination of Plasmin Inhibitory Activity

The inhibition ratio was found by the fibrin plate method. Specifically, the fibrin plate was made by the method of Astrup et al. (Arch.Biochem; 40, 346, 1952) and test material prepared as described above was diluted with ethanol to 0.1% and 0.01% and used. The results are shown in Table 3.

[0029] (3) Determination of Trypsin Inhibitory Activity

The inhibition ratio was found by the method of Muramatu [sic] et al. with casein as the substrate (J. Biochem.; 58, 214, 1965). The test material was diluted in the same way to 0.1% and 0.01% and used. The results are shown in Table 3. In addition, as reference examples, the same test as described above was performed on ethanol extracts of Kunyit (scientific name: *Curcuma domestica*) of the family *Zingiberaceae*, Lempuyang (scientific name: *Zingiber aromaticum* Mal.) of the family *Zingiberaceae* and mugwort, which are plants known to be applied for skin roughness. The results are shown in Table 3.

[0030]

[Table 3]

	Concentration of Test Material Added	Inhibition ratio (%)	
		Plasmin	Trypsin
Buah tempayang	0.1%	46.3	40.0
	0.01%	22.9	20.1
Kunyit	0.1%	3.0	0
	0.01%	0	0
Lempuyang	0.1%	0	0
	0.01%	0	0
Mugwort	0.1%	18.6	0
	0.01%	5.8	0

[0031] 2. Tests of Roughness Improving Effect

(1) Actual Use Test

The effects of topical application of the topical agent of this invention were evaluated from the improvement ratios for skin roughness, razor load and pigment deposition and from skin irritability. The faces of a panel of 60 women suffering from skin roughness was used. Test materials from the lotions of the compositions (weight %) shown in Table 4 were applied twice a day for 2 weeks to one cheek on either the right or left side and the control was applied to the cheek on the other side, after which the state of the skin was evaluated visually. A panel of 30 men with shaving load were used as subjects, lotions of the compositions shown in Table 4 were applied immediately after shaving and the effect on razor load were evaluated. The evaluation standards are as indicated below. The test materials, with products of this invention, were two Buah tempayang methanol extracts the concentrations of which were varied and the comparison products were substances in which were compounded methanol extracts of Kunyit (scientific name: *Curcuma domestica*) of the family *Zingiberaceae*, Lempuyang (scientific name: *Zingiber aromaticum* Mal.) of the family *Zingiberaceae* and mugwort, which are plants

known to be applied for skin roughness. The results are shown in Table 5.

[0032] (1) Standards of Evaluation of Improving Effects on Skin Roughness

Markedly effected: Cases in which symptoms disappeared.

Effective: Cases in which symptoms were weakened.

Somewhat effective: Cases in which symptoms were somewhat weakened.

Ineffective: Cases in which changes in symptoms were not found.

[0033] (2) Standard of Evaluation of Improving Effects on Razor Load

Markedly effective: Cases in which razor load was eliminated.

Effective: Cases in which razor load was weakened.

Somewhat effective: Cases in which razor load was somewhat weakened.

Ineffective: Cases in which changes in razor load were not found.

[0034] (3) Improving Effect on Skin Roughness and Razor Load

Ø: Proportion of subjects for whom findings of markedly effective, effective and somewhat effective (efficacy rate) was 80% or greater

O: Proportion of subjects for whom findings of markedly effective, effective and somewhat effective (efficacy rate) was 50 to 80%

Δ: Proportion of subjects for whom findings of markedly effective, effective and somewhat effective (efficacy rate) was 30% to 50%

×: Proportion of subjects for whom findings of markedly effective, effective and somewhat effective (efficacy rate) was 30% or less

[0035] (4) Skin Irritability

Ø: Proportion of subjects exhibiting smarting sensation of the skin was 0%.

O: Proportion of subjects exhibiting smarting sensation of the skin was less than 5%.

Δ: Proportion of subjects exhibiting smarting sensation of the skin was less than 10%.

×: Proportion of subjects exhibiting smarting sensation of the skin was greater than 10%.

**[0036]
[Table 4]**

Test Material	Products of this Invention		Comparison Products	
	1	2	1	2
Methanol extract of Buah tempayang	1.0	0.5	-	-
Methanol extract of Kunyit	-	-	1.0	-
Methanol extract of Lempuyang	-	-	-	1.0
Glycerol	10.0	10.0	10.0	10.0
1,3-butylene glycol	4.0	4.0	4.0	4.0
Ethanol	7.0	7.0	7.0	7.0
Polyoxyethylene (20 mol) oleyl alcohol	0.5	0.5	0.5	0.5
Purified water	Remainder	Remainder	Remainder	Remainder

[0037] [Table 5]

Test Material	Products of this Invention		Comparison Products	
	1	2	1	2
Improving effect on skin roughness	Ø	O	Δ	Δ
Effect in preventing razor load	Ø	O	Δ	Δ
Skin irritability	Ø	Ø	O	Δ

[0038] As should be evident from Table 5, test materials of this invention in which Buah tempayang extract was compounded exhibited improving effects on skin roughness and razor load superior to those of the test materials of the comparison products. Moreover, skin irritability was not found.

[0039] (2) Actual Tests by the Replica Method

Skin roughness improving tests were performed on a panel of human subjects using lotions of products 1 and 2 of this invention and of comparison products 1 and 2. Specifically, skin replicas were collected using the replica method with myristone resin and the state of the skin surface of normal healthy women was observed under the microscope

(magnification of 17 times). Evaluations of skin roughness were made on the basis of the standards shown in Table 6 from the state of skin crests and from the state of exfoliation of keratin by applying lotions of products 1 and 2 of this invention and comparison products 1 and 2 twice a day for two weeks on the right and left halves of the faces of 20 individuals (skin roughness panel) evaluated for 1 or 2. After 2 weeks, the state of the skin was observed by the replica method as described above and evaluations were made according to the evaluation standards in Table 6. The results are shown in Table 7.

**[0040]
[Table 6]**

Score	Score Standards
1	Elimination of skin grooves and skin crests and tearing off of keratin over a broad range are found.
2	Skin grooves and crests are not distinct and tearing off of keratin is found.
3	Skin grooves and crests are found but are flat.
4	Skin grooves and crests are distinct.
5	Skin grooves and crests are distinct and regular.

[0041]

[Table 7]

Replica Evaluation	Product 1 of the Invention	Product 2 of the Invention	Comparison Product 1	Comparison Product 2
1	0	0	1	0
2	0	1	3	4
3	4	6	13	11
4	15	15	3	5
5	1	0	0	0

[0042] As can be seen from Table 7, it was found that the lotions that were a product of this invention had a markedly more improved roughness softening effect than the lotions that were comparison products.

[0043] Working Example 1. Cream

(Formulation)

Stearic acid	5.0	weight %
Stearyl alcohol	4.0	
Isopropyl myristate	18.0	
Glycerol monostearic acid ester	3.0	
Propylene glycol	10.0	
Buah tempayang methanol extract	0.01	
Sodium hydroxide	0.2	

Sodium hydrogen sulfite

0.01

Preservative

suitable quantity

Fragrance

suitable quantity

Ion exchange water

remainder

(Preparation method) The propylene glycol, Buah tempayang methanol extract and sodium hydroxide were added to and dissolved in the ion exchange water and the solution was heated and maintained at 70°C (aqueous phase). The other components were mixed and fused by heating and the solution was maintained at 70°C (oleaginous phase). The oleaginous phase was gradually added to the aqueous phase. After it had been completely added, the temperature was maintained and a reaction was brought about. Following that, the product was emulsified to a homogeneous state with a homomixer and was cooled to 30° as it was being vigorously stirred.

[0044]

Working Example 2. Cream

(Formulation)

Stearic acid	2.0	weight %
Stearyl alcohol	7.0	
Hydrogenated lanolin	2.0	
Squalane	5.0	
2-octyldodecyl alcohol	6.0	
Polyoxyethylene (25 mol) cetyl alcohol ether	3.0	
Glycerol monostearic acid ester	2.0	
Propylene glycol	5.0	
Buah tempayang ethanol extract	0.05	
Sodium hydrogen sulfite	0.03	
Ethyl paraben	0.3	
Fragrance	suitable quantity	
Ion exchange water	remainder	

(Preparation method) The propylene alcohol was added to the ion exchange water and the mixture was heated and maintained at 70°C (aqueous phase). The other components were added and fused by heating and maintained at 70°C

(oleaginous phase). The oleaginous phase was added to the aqueous phase and the mixture was subjected to preliminary emulsification, after which it was cooled to 30°C as it was being vigorously stirred.

[0045]

Working Example 3. Cream

(Formulation)

Solid paraffin	5.0	weight %
Beeswax	10.0	
Vaseline	15.0	
Liquid paraffin	41.0	
Glycerol monostearic acid ester	2.0	
Polyoxyethylene (20 mol) sorbitan monolauric acid ester	2.0	

Soap powder	0.1
Borax	0.2
Buah tempayang acetone extract	0.1
Sodium hydrogen sulfite	0.03
Ethyl paraben	0.3
Fragrance	suitable quantity
Ion exchange water	remainder

(Preparation method) The soap powder and borax were added to the ion exchange water and the mixture was heated and maintained at 70°C (aqueous phase). The other components were added and fused by heating and maintained at 70°C (oleaginous phase). The oleaginous phase was added to the aqueous phase and a reaction was carried out as the mixture was being stirred. After the reaction was completed, the

product was emulsified to a homogeneous state with a homomixer. After emulsification, it was cooled to 30°C as it was being vigorously stirred.

[0046]

Working Example 4. Emulsion

(Formulation)

Stearic acid	2.5	weight %
Cetyl alcohol	1.5	
Vaseline	5.0	
Liquid paraffin	10.0	
Polyoxyethylene (10 mol) monooleic acid ester	2.0	
Polyethylene glycol 1500	3.0	
Triethanolamine	1.0	
Carboxyvinyl polymer	0.05	
(Brand name: Carbopol 941, B.F. Goodrich Chemical Company)		
Buah tempayang ethyl acetate ester extract	0.01	
Sodium hydrogen sulfite	0.01	
Ethyl paraben	0.3	
Fragrance	suitable quantity	
Ion Exchange water	remainder	

(Preparation method) The carboxy vinyl polymer was dissolved in a small quantity of ion exchange water (phase A). Polyethylene glycol 1500 and triethanolamine were added to the remaining ion exchange water and dissolved by heating and maintained at 70°C (aqueous phase). The other components were mixed, fused by heating and maintained at 70°C (oleaginous phase). The oleaginous phase was added to the aqueous phase and preliminary emulsification was

performed. Phase A was added and emulsification was effected to a homogeneous state in a homomixer. After emulsification, the product was cooled to 30°C as it was being vigorously stirred.

[0047]

Working Example 5. Emulsion

(Formulation)

Microcrystalline beeswax	1.0	weight %
Beeswax	2.0	
[Translator's Note: Characters say "dense wax." The character for "dense" has the same pronunciation as the character for "bee" and is therefore interpreted as a misprint.]		
Lanolin	20.0	
Liquid paraffin	10.0	
Squalane	5.0	
Sorbitan sesquioleic acid ester	4.0	
Polyoxyethylene (20 mol) sorbitan monooleic acid ester	1.0	
Propylene glycol	7.0	
Buah tempayang acetone extract	10.0	
Sodium hydrogen sulfite	0.01	

Ethyl paraben	0.3
Fragrance	suitable quantity
Ion exchange water	remainder

(Preparation method) The propylene glycol was added to the ion exchange water, heated and maintained at 70°C (aqueous phase). The other components were mixed, fused by heating and maintained at 70°C (oleaginous phase). The aqueous phase was added as the oleaginous phase was being stirred

and the mixture was emulsified to a homogeneous state with a homomixer. After emulsification, it was cooled to 30°C as it was being vigorously stirred.

[0048]

Working Example 6. Jelly

(Formulation)

95% ethyl alcohol	10.0	weight %
Dipropylene glycol	15.0	
Polyoxyethylene (50 mol) oleyl alcohol ether	2.0	
Carboxyvinyl polymer	1.0	
(Brand name: Carbopol 940, B.F. Goodrich Chemical Company)		
Sodium hydroxide	0.15	
L-arginine	0.1	
Buah tempayang 50% ethanol aqueous solution extract	7.0	
Sodium 2-hydroxy-4-methoxybenzophenone stearate	0.05	
Ethylenediamine tetraacetate · trisodium · dihydride	0.05	
Ethyl paraben	0.2	
Fragrance	suitable quantity	
Ion exchange water	remainder	

(Preparation method) The Carbopol 940 was dissolved to a homogeneous state in the ion exchange water. Separately, the Buah tempayang 50% ethanol aqueous solution extract and the Polyoxyethylene (50 mol) oleyl alcohol ether were dissolved in 95% ethanol and the solution was added to the

aqueous phase. Next, the other components were added, after which the mixture was neutralized and thickened with sodium hydroxide and L-arginine.

[0049]

Working Example 7. Beautifying solution

(Formulation)

(Phase A)

Ethyl alcohol (95%)	10.0	weight %
Polyoxyethylene (20 mol) octyl dodecanol	1.0	
Pantothenyl ethyl ether	0.1	
Buah tempayang methanol extract	1.5	
Methyl paraben	0.15	

(Phase B)

Potassium hydroxide	0.1
---------------------	-----

(Phase C)

Vaseline	5.0
Dipropylene glycol	10.0
Sodium hydrogen sulfite	0.03
Carboxyvinyl polymer	0.2

(Brand name: Carbopol 940, B.F. Goodrich Chemical Company)

Purified water	remainder
----------------	-----------

(Preparation method) Phase A and phase C, respectively, were dissolved to homogeneous states, phase A was added to

phase C and the mixture was solubilized. Next, phase B was added, after which filling was performed.

[0050] Working Example 8. Pack

(Formulation)

(Phase A)

Propylene glycol	5.0	weight %
Polyoxyethylene (60 mol) hardened castor oil	5.0	

(Phase B)

Buah tempayang methanol extract	0.01
Olive oil	5.0
Tocopherol acetate	0.2
Ethyl paraben	0.2

Fragrance	0.2
(Phase C)	
Sodium hydrogen sulfite	0.03
Polyvinyl alcohol	13.0
(degree of gelation, 90; degree of polymerization, 2000)	
Ethanol	7.0
Purified water	remainder

(Preparation method) Phase A and phase C, respectively, were dissolved to homogeneous states, phase B was added to phase A and the mixture was solubilized. Next, phase C was added, after which filling was performed.

[0051] Working Example 9. Solid foundation

(Formulation)

Talc	43.1	weight %
Kaolin	15.0	
Celesite	10.0	
Zinc white	7.0	
Titanium dioxide	3.8	
Yellow iron oxide	2.9	
Black iron oxide	0.2	
Squalane	8.0	
Isostearic acid	4.0	
Monostearic acid POE sorbitan	3.0	
Isocetyl octanoate	2.0	
Buah tempayang ethanol extract	1.0	
Preservative	suitable quantity	
Fragrance	suitable quantity	

(Preparation method) The powdered components, talc ~ black iron oxide, were thoroughly mixed in a blender, the oleaginous components, squalane ~ isocetyl octanoate, the Buah tempayang ethanol extract, the preservative and the fragrance were added and thoroughly kneaded, after which the mixture was fed into a container and molded.

[0052]

Working Example 10. Emulsified foundation (cream type)

(Formulation)

(Powder component)		
Titanium dioxide	10.3	weight %
Celesite	5.4	
Kaolin	3.0	
Yellow iron oxide	0.8	
Red oxide of iron	0.3	
Black iron oxide	0.2	
(Oleaginous phase)		
Decamethylcyclpentasiloxane	11.5	
Liquid paraffin	4.5	
Polyoxyethylene modified dimethyl polysiloxane	4.0	
(Aqueous phase)		
Purified water	50.0	
1,3-butylene glycol	4.5	
Buah tempayang ethanol extract	1.5	
Sorbitan sesquioleic acid ester	3.0	
Preservative	suitable quantity	
Fragrance	suitable quantity	

(Preparation method) The aqueous phase was heated and stirred, after which the powder components, which had been thoroughly mixed and pulverized, were added and homomixer treatment was performed. Further, the oleaginous phase, which had been heated and mixed, was added and homomixer treatment was performed, after which the fragrance was added as the mixture was being stirred and the product was cooled to room temperature.

[0053]

[Effect of the Invention] As described above, the skin agent for topical use of this invention has a melanin production inhibiting action and a tyrosinase activity inhibiting action, it has superior effects in pigment deposition after sunburn, lightening the color and whitening of spots, freckles and liver spots and has superior effects in various skin diseases and in improving skin roughness and chapping.

Continued from front page

(51) Int.Cl. ⁶	Ident. Symbols	Internal Office Nos.	FI				Technology Indication
A61K 35/78	ADS		A61K 35/78	K		ADS	
	AED					AEDC	
C12N 9/99			C12N 9/99				
(72) Inventor:	Yoshiro Yokogawa c/o First Research Center, Shiseido Company, Ltd. 1050 Nitsuba-cho, Kohoku-ku, Yokohama-shi, Kanagawa-ken			(72) Inventor:	Kanemoto Kitamura c/o First Research Center, Shiseido Company, Ltd. 1050 Nitsuba-cho, Kohoku-ku, Yokohama-shi, Kanagawa-ken		